

Application No.
Amendment Dated
Reply to Office Action of

13/550,038
03/31/2006
03/22/2006

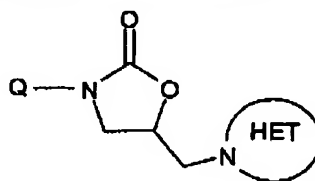
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In the Claims

The listing of claims will replace all prior versions and listings of claims in the application.

Listings of claim

1. (Currently Amended) A compound of the formula (I), or a pharmaceutically-acceptable salt, or an in-vivo-hydrolysable ester thereof,



(I)

wherein -N-HET is selected from the structures (Ia) to (If) below :-



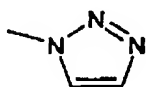
(Ia)



(Ib)



(Ic)



(Id)

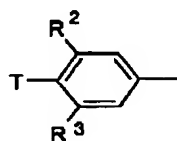


(Ie)

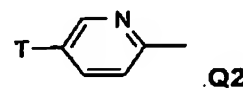


(If)

Q is selected from Q1 to Q6



Q1 or



Q2



Q3



Q4



Q5



Q6

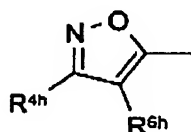
R₂ and R₃ are independently selected from H, F, Cl, CF₃, OMe, SMe, Me and Et;

B₁ is O or S;

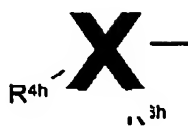
T is selected from the groups in (TAa1) to (TAa12):

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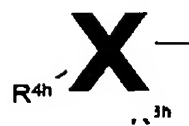
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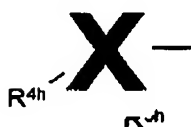
(TAa1)



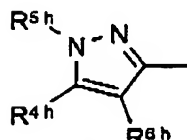
(TAa2)



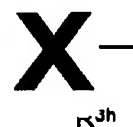
(TAa3)



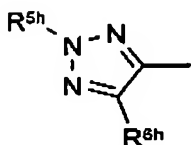
(TAa4)



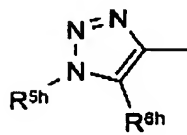
(TAa5)



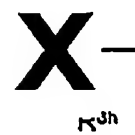
(TAa6)



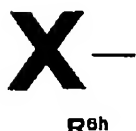
(TAa7)



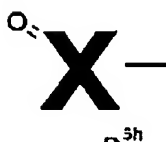
(TAa8)



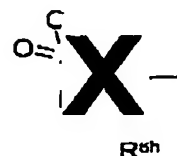
(TAa9)



(TAa10)



(TAa11)



(TAa12)

wherein :

R^{6h} is hydrogen or (1-4C)alkyl;

R^{4h} and R^{5h} are independently selected from hydrogen, cyano, hydroxy(1-4C)alkyl, cyano(1-4C)alkyl, phosphoryl(1-4C)alkyl, benzyl (optionally substituted on the phenyl ring by one substituent selected from halo, methyl and methoxy), (1-4C)alkyl, (1-4C)alkyl substituted with ORc (wherein Rc is $R^{13}CO$ and R^{13} is selected from Rc2b), (1-4C)alkanoyl and (1-4C)alkoxycarbonyl.

R^{6h} is selected from hydrogen, (1-4C)alkyl, (1-4C)alkoxycarbonyl, (1-4C)alkanoyl, carbamoyl and cyano;

R^{4h} and R^{5h} are independently selected from hydrogen, halo, trifluoromethyl, cyano, nitro, (1-4C)alkoxy, (1-4C)alkylS(O)_q (q is 0, 1 or 2), (1-4C)alkanoyl, (1-4C)alkoxycarbonyl, benzyloxy (1-4C)alkyl, (2-4C)alkanoylamino, CONR_cR_v and NR_cR_v wherein any (1-4C)alkyl group contained in the preceding values for R^{4h} and R^{5h} is optionally substituted by

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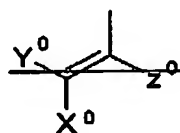
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up to three substituents independently selected from hydroxy (not on C1 of an alkoxy group, and excluding geminal disubstitution), oxo, trifluoromethyl, cyano, nitro, (1-4C)alkoxy, (2-4C)alkanoyloxy, hydroxyimino, (1-4C)alkoxyimino, (1-4C)alkylS(O)_q (q is 0, 1 or 2), (1-4C)alkylSO₂-NR_v, (1-4C)alkoxycarbonyl, CONR_eR_v, and NR_eR_v (not on C1 of an alkoxy group, and excluding geminal disubstitution); wherein R_v is hydrogen or (1-4C)alkyl and R_e is as hereinafter defined;

R^{4h} and R^{6h} may further be independently selected from (1-4C)alkyl (optionally substituted by one, two or three substituents independently selected from hydroxy (excluding geminal disubstitution), oxo, trifluoromethyl, cyano, nitro, (1-4C)alkoxy, (2-4C)alkanoyloxy, phosphoryl [-O-P(O)(OH)₂], and mono and di (1-4C)alkoxy derivatives thereof], phosphinyl [-O-P(OH)₂], and mono and di (1-4C)alkoxy derivatives thereof], hydroxyimino, (1-4C)alkoxyimino, (1-4C)alkylS(O)_q (q is 0, 1 or 2), (1-4C)alkylSO₂-NR_v, (1-4C)alkoxycarbonyl, CONR_eR_v, NR_eR_v (excluding geminal disubstitution), OR_e, and phenyl (optionally substituted by one, two or three substituents independently selected from (1-4C)alkyl, (1-4C)alkoxy and halo)); wherein R_v is hydrogen or (1-4C)alkyl and R_e is as hereinafter defined; and wherein any (1-4C)alkyl group contained in the immediately preceding optional substituents (when R^{4h} and R^{6h} are independently (1-4C)alkyl) is itself optionally substituted by up to three substituents independently selected from hydroxy (not on C1 of an alkoxy group, and excluding geminal disubstitution), oxo, trifluoromethyl, cyano, nitro, (1-4C)alkoxy, (2-4C)alkanoyloxy, hydroxyimino, (1-4C)alkoxyimino, (1-4C)alkylS(O)_q (q is 0, 1 or 2), (1-4C)alkylSO₂-NR_v, (1-4C)alkoxycarbonyl, CONR_eR_v, and NR_eR_v (not on C1 of an alkoxy group, and excluding geminal disubstitution); wherein R_v is hydrogen or (1-4C)alkyl and R_e is as hereinafter defined;

or R^{4h} is selected from one of the groups in (TAaa) to (TAab) below, or (where appropriate) one of R^{4h} and R^{6h} is selected from the above list of R^{4h} and R^{6h} values, and the other is selected from one of the groups in (TAaa) to (TAab) below:-

(TAaa)—a group of the formula (TAaa1)



(TAaa1)

wherein Z⁰ is hydrogen or (1-4C)alkyl;

X⁰ and Y⁰ are independently selected from hydrogen, (1-4C)alkyl, (1-4C)alkoxycarbonyl, halo, cyano, nitro, (1-4C)alkylS(O)_q (q is 0, 1 or 2), R_vR_wNSO₂, trifluoromethyl,

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~~pentafluoroethyl, (1-4C)alkanoyl and CONR_vR_w [wherein R_v is hydrogen or (1-4C)alkyl;
 R_w is hydrogen or (1-4C)alkyl];~~

~~(TAab) an acetylene of the formula \equiv H or \equiv (1-4C)alkyl;~~

~~wherein R_c is selected from groups (Rc1) to (Rc2) :-~~

~~(Rc1) (1-6C)alkyl (optionally substituted by one or more (1-4C)alkanoyl groups (including geminal disubstitution) and/or optionally monosubstituted by cyano, (1-4C)alkoxy, trifluoromethyl, (1-4C)alkoxycarbonyl, phenyl (optionally substituted as for AR1 defined hereinafter), (1-4C)alkylS(O)_q (q is 0, 1 or 2); or, on any but the first carbon atom of the (1-6C)alkyl chain, optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy and fluoro, and/or optionally monosubstituted by oxo, NR_vR_w [wherein R_v is hydrogen or (1-4C)alkyl; R_w is hydrogen or (1-4C)alkyl], (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylS(O)_pNH or (1-4C)alkylS(O)_p((1-4C)alkyl)N (p is 1 or 2));~~
~~(Rc2) R¹³CO-, R¹³SO₂- or R¹³CS-~~

~~wherein R¹³ is selected from (Rc2a) to (Rc2d) :-~~

~~(Rc2a) hydrogen, (1-4C)alkoxycarbonyl, trifluoromethyl and NR_vR_w [wherein R_v is hydrogen or (1-4C)alkyl; R_w is hydrogen or (1-4C)alkyl];~~

~~(Rc2b) (1-10C)alkyl~~

~~{optionally substituted by one or more groups (including geminal disubstitution) each independently selected from hydroxy, (1-10C)alkoxy, (1-4C)alkoxy-(1-4C)alkoxy, (1-4C)alkoxy-(1-4C)alkoxy-(1-4C)alkoxy, (1-4C)alkanoyl, carboxy, phosphoryl [-O-P(O)(OH)₂, and mono- and di-(1-4C)alkoxy derivatives thereof], phosphiryl [-O-P(OH)₂ and mono- and di-(1-4C)alkoxy derivatives thereof], and amino; and/or optionally substituted by one group selected from phosphonate [phosphono, -P(O)(OH)₂, and mono- and di-(1-4C)alkoxy derivatives thereof], phosphinate [-P(OH)₂ and mono- and di-(1-4C)alkoxy derivatives thereof], cyano, halo, trifluoromethyl, (1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxy-(1-4C)alkoxycarbonyl, (1-4C)alkylamino, di((1-4C)alkyl)amino, (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylaminocarbonyl, di((1-4C)alkyl)aminocarbonyl, (1-4C)alkylS(O)_pNH-, (1-4C)alkylS(O)_p((1-4C)alkyl)N-, fluoro(1-4C)alkylS(O)_pNH-, fluoro(1-4C)alkylS(O)_p((1-4C)alkyl)N-, (1-4C)alkylS(O)_q [the (1-4C)alkyl group of (1-4C)alkylS(O)_q being optionally substituted by one substituent selected from hydroxy, (1-4C)alkoxy, (1-4C)alkanoyl, phosphoryl [-O-P(O)(OH)₂, and mono- and di-(1-4C)alkoxy derivatives thereof], phosphiryl [-O-P(OH)₂ and mono- and di-(1-4C)alkoxy derivatives thereof], amino, cyano, halo, trifluoromethyl, (1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxycarbonyl, (1-4C)alkoxy-(1-4C)alkoxy-(1-4C)alkoxycarbonyl, carboxy, (1-4C)alkylamino, di((1-~~

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4C)alkyl)amino, (1-6C)alkanoylamino, (1-4C)alkoxycarbonylamino, N-(1-4C)alkyl-N-(1-6C)alkanoylamino, (1-4C)alkylaminocarbonyl, di((1-4C)alkyl)aminocarbonyl, (1-4C)alkylS(O)_pNH-, (1-4C)alkylS(O)_p-((1-4C)alkyl)N-, and (1-4C)alkylS(O)_q;

~~(Re2e) — R⁴⁴C(O)O(1-6C)alkyl wherein R⁴⁴ is AR1, AR2, (1-4C)alkylamino (the (1-4C)alkyl group being optionally substituted by (1-4C)alkoxycarbonyl or by carboxy), benzyloxy (1-4C)alkyl or (1-10C)alkyl (optionally substituted as defined for (Re2b));~~

~~(Re2d) — R⁴⁶O wherein R⁴⁶ is benzyl, (1-6C)alkyl (optionally substituted as defined for (Re2c)) or AR2b;~~

wherein

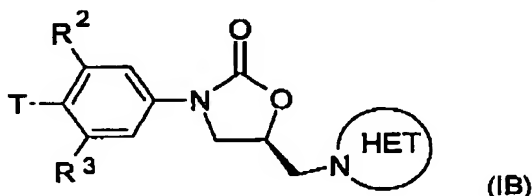
~~AR1 is an optionally substituted phenyl or optionally substituted naphthyl;~~

~~AR2 is an optionally substituted 5- or 6-membered, fully unsaturated monocyclic heteroaryl ring containing up to four heteroatoms independently selected from O, N and S (but not containing any O-O, O-S or S-S bonds), and linked via a ring carbon atom, or a ring nitrogen atom if the ring is not thereby quaternised;~~

~~AR2a is a partially hydrogenated version of AR2, linked via a ring carbon atom or linked via a ring nitrogen atom if the ring is not thereby quaternised;~~

~~AR2b is a fully hydrogenated version of AR2, linked via a ring carbon atom or linked via a ring nitrogen atom.~~

2. (Previously Presented) A The compound of claim 1, wherein Q is Q1.
3. (Cancelled)
4. (Previously Presented) The compound of claim 1, wherein R² and R³ are independently hydrogen or fluoro.
5. (Cancelled)
6. (Currently Amended) The compound of claim 1, which is a compound of formula (IB)



wherein -N-HET is 1,2,3-triazo-1-yl or tetrazol-2-yl;

R² and R³ are independently hydrogen or fluoro;

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T is selected from TAA1, TAA5, TAA7 and TAA8;

R^{6h} is hydrogen or (1-4C)alkyl;

R^{4h} and R^{5h} are independently selected from hydrogen, cyano, hydroxy(1-4C)alkyl, cyano(1-4C)alkyl, phosphoryl(1-4C)alkyl, benzyl (optionally substituted on the phenyl ring by one substituent selected from halo, methyl and methoxy), (1-4C)alkyl, (1-4C)alkyl substituted with ORc (wherein Rc is R¹³CO and R¹³ is selected from Rc2b), (1-4C)alkanoyl and (1-4C)alkoxycarbonyl.

7. (Cancelled)

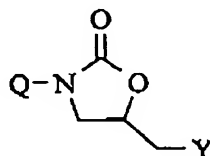
8. (Previously Presented) A method for producing an antibacterial effect in a warm blooded animal which comprises administering to said animal an effective amount of a compound of claim 1.

9 – 10. (Cancelled)

11. (Previously Presented) A pharmaceutical composition which comprises a compound of claim 1, and a pharmaceutically-acceptable diluent or carrier.

12. (Original) A process for the preparation of a compound of formula (I) as claimed in claim 1 or pharmaceutically acceptable salts or in-vivo hydrolysable esters or pro-drugs thereof, which process comprises one of processes (a) to (g):

- (a) by modifying a substituent in, or introducing a new substituent into, the substituent group Q of another compound of formula (I); or
- (b) by reaction of a compound of formula (II):



(II)

wherein Y is a displaceable group with a compound of the formula (III):



(III)

wherein -N-HET (of formula (Ia) to (If) optionally protected) is HN-HET (free-base form) or N-HET anion formed from the free base form; or

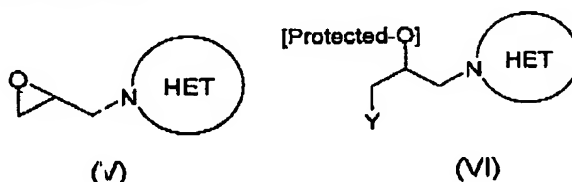
- (c) by reaction of a compound of the formula (IV):

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Q-Z

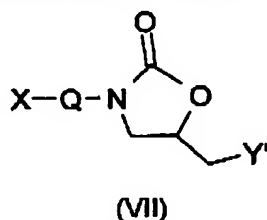
(IV)

wherein Z is an isocyanate, amine or urethane group with an epoxide of the formula (V) wherein the epoxide group serves as a leaving group at the terminal C-atom and as a protected hydroxy group at the internal C-atom; or with a related compound of formula (VI) where the hydroxy group at the internal C-atom is protected and where the leaving group Y at the terminal C-atom is a leaving group;

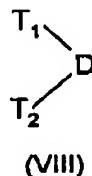


or

(d) (i) by coupling, using catalysis by transition metals, of a compound of formula (VII) :



wherein Y' is a group -N-HET as hereinbefore defined, X is a replaceable substituent; with a compound of the formula (VIII), or an analogue thereof, which is suitable to give a T substituent as defined by (TAa1-TAa12) in which the link is via an sp² carbon atom (D = CH=C-Lg where Lg is a leaving group; or as in the case of reactions carried out under Heck reaction conditions Lg may also be hydrogen)

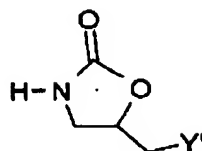


where T₁ and T₂ may be the same or different and comprise a precursor to a ring of type T as hereinbefore defined, or T₁ and T₂ may together with D form a ring of type T as hereinbefore defined;

(d) (ii) by coupling, using catalysis by transition metals, of a compound of formula (VIIA):

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(VIIA)

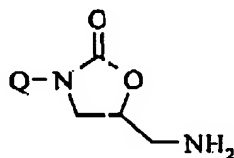
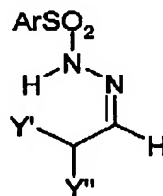
wherein Y' is a group HET as hereinbefore defined, with a compound

[Aryl]-X

where X is a replaceable substituent;

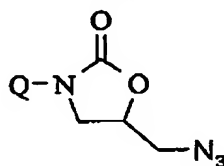
(e) Where N-HET is 1,2,3-triazole by cycloaddition via the azide (wherein Y in (II) is azide), with acetylene or masked acetylene;

(f) Where N-HET is 1,2,3-triazole by synthesis with a compound of formula (IX), namely the arenesulfonylhydrazone of acetaldehyde, by reaction of a compound of formula (II) where Y = NH₂ (primary amine);

(II : Y = NH₂)

(IX)

(g) Where N-HET is 1,2,3-triazole by cycloaddition via the azide (wherein Y in (II) is azide) with acetylene using Cu(I) catalysis in to give the N-1,2,3-triazole;

(II : Y = N₃)

and thereafter if necessary :

- i) removing any protecting groups;
- ii) forming a pro-drug (for example an in-vivo hydrolysable ester); and/or
- iii) forming a pharmaceutically acceptable salt.

13. (Previously Presented) A compound which is

(5*R*)-3-{3-Fluoro-4-(3-methylisoxazol-5-yl)phenyl}-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one;

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Ethyl 5-{2-fluoro-4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}isoxazole-3-carboxylate;

(5*R*)-3-[3-Fluoro-4-[3-(hydroxymethyl)isoxazol-5-yl]phenyl]-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one;

(5-{2-Fluoro-4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}isoxazol-3-yl)methyl dihydrogen phosphate;

1-Methyl-3-[4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl]-1*H*-pyrazole-5-carbonitrile;

1-Methyl-3-[4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl]-1*H*-pyrazole-5-carbaldehyde;

(5*R*)-3-[3-Fluoro-4-(1*H*-1,2,3-triazol-4-yl)phenyl]-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one;

(5*R*)-3-[3-Fluoro-4-(1-methyl-1*H*-1,2,3-triazol-4-yl)phenyl]-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one;

(5*R*)-3-[3-Fluoro-4-(2-methyl-2*H*-1,2,3-triazol-4-yl)phenyl]-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-2-one;

(4-{2-Fluoro-4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}-1*H*-1,2,3-triazol-1-yl)acetonitrile; or

(4-{2-Fluoro-4-[(5*R*)-2-oxo-5-(1*H*-1,2,3-triazol-1-ylmethyl)-1,3-oxazolidin-3-yl]phenyl}-2*H*-1,2,3-triazol-2-yl)acetonitrile.

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